UNITED STATES DISTRICT COURT
DISTRICT OF NEW JERSEY

ROCHE PALO ALTO LLC, GILEAD PALO ALTO, INC. and GILEAD SCIENCES, INC. Plaintiffs, v. LUPIN LTD., and LUPIN PHARMACEUTICALS, INC. Defendants.	Civil Action No. 2:10-cv-03561 (ES/SCM)

PLAINTIFFS' POST-TRIAL RESPONSIVE CLAIM CONSTRUCTION BRIEF REGARDING "RANOLAZINE PLASMA LEVELS" LIMITATIONS

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Dated: June 14, 2013

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I. INTRODUCTION

The specification resolves the parties' dispute about whether the claimed plasma values are mean values or individual values. The asserted claims refer to "ranolazine plasma levels" in terms of "ng base/mL"—a concentration. The specification unambiguously states that plasma ranolazine concentration is a mean value:

> Plasma ranolazine concentration is a ***mean*** concentration determined by analyzing the concentration of ranolazine in as few as five to as many as ten humans who are on the same dosing schedule. ***It is important that the ranolazine concentration is a mean value*** because of variances in ranolazine concentrations in individuals that may be caused by differences in weight, metabolism, or disease states which may cause one person to metabolize ranolazine faster or slower than an average person. The plasma ranolazine levels are determined from drawn blood onto heparin.

(PTX 21, '258 Patent Col. 3:38-47 (emphasis added).)

Realizing that its "individual patient" construction is at odds with this explicit statement in the specification, Lupin strains to argue that the specification distinguishes "plasma ranolazine concentrations" from "plasma ranolazine levels" with the former being a mean value and the latter being an individual value. Lupin's argument is threadbare. Nothing in the specification suggests a "ranolazine concentration" differs in any way from a "ranolazine level." Nor is there anything in the specification to suggest that "ranolazine concentrations" are mean values but "ranolazine levels" are individual values. Lupin's resort to such semantics highlights that its "individual patient" construction is incorrect. Lupin's construction should be rejected.

II. ARGUMENT

As an initial matter, Lupin is incorrect in arguing that this is a lexicography case. The lexicography cases typically involve a patentee "redefining" the meaning of claim terms "away from their ordinary meaning." *See, e.g., Merck & Co. v. Teva Pharm. USA Inc.*, 395 F.3d 1364, 1370 (Fed. Cir. 2005). Here, the inventors have not redefined a term away from its ordinary

meaning. While the inventors satisfied the lexicography standard of "reasonable clarity, deliberateness, and precision" when defining "plasma ranolazine concentration," the specification's definition is consistent with the ordinary meaning. *Id*. at 1378.

As explained in Plaintiffs' opening brief, in the context of pharmacokinetic data, it is customary to employ mean values for "plasma levels" or "plasma concentration." (Opening Br. at 2.) Moreover, as far as the interpretation of the articles "a" and "the" in patent claims, these terms do not invoke a singular meaning. (Opening Br. at 4; *see e.g.*, *Baldwin Graphic Sys., Inc. v. Siebert*, Inc., 512 F.3d 1338, 1342 (Fed. Cir. 2008).) In this regard, Dr. Weiner did not, as Lupin asserts, "admit" that the claims relate to "a single human patient." Rather, he merely stated the obvious—doctors treat individuals. He proceeded to testify that, in context, the claimed plasma levels relate to mean values, consistent with how scientists typically assess pharmacokinetic properties. (4/30/13 Trial Tr. at 44:19-47:14 (Weiner).)

The inventors' explicit definition is thus consistent with both how pharmacokinetic data are customarily expressed and how the articles "a" and "the" are generally understood. Plaintiffs' acknowledge, however, that not all courts have found that the ordinary meaning of claims terms directed to pharmacokinetic values in "a patient" is a mean value. As discussed in their opening brief, the *Wyeth v. Lupin* court found that the ordinary meaning of "in a patient" referred to an individual value, but then proceeded to construe the term as a mean value because "the plain meaning of the terms does not lead to correct claim construction." *Wyeth v. Lupin LTD*, 579 F. Supp. 2d 711, 719 (D. Md. 2008).

This highlights the importance of the specification, particularly in this case, in construing the ranolazine plasma level terms. The specification "is always highly relevant to the claim construction analysis" and "is the single best guide to the meaning of a disputed term." *Phillips*

v. AWH Corp., 415 F.3d 1303, 1314 (Fed. Cir. 2005) (quoting *Vitronics Corp. v. Conceptronic, Inc.*, 90 F.3d 1576, 1582 (Fed. Cir. 1996)). Here, the specification is dispositive. It explicitly states that "[p]lasma ranolazine concentration is a mean concentration" and that "[i]t is important that the ranolazine concentration is a mean value." (PTX 21, '258 Patent Col. 3:38-43.)

Faced with the specification's explicit statement, Lupin grasps onto the last sentence of the "Plasma ranolazine concentration" definitional paragraph which states "[t]he plasma ranolazine levels are determined from drawn blood onto heparin" and argues that 1) the specification is somehow drawing a distinction between "ranolazine levels" and "ranolazine concentration" and 2) because blood is drawn from individuals, "ranolazine levels" must refer to individual values. Lupin's argument is unreasonable.

First, the specification draws no distinction between "ranolazine concentration" and "ranolazine levels." The "plasma ranolazine levels" in the quote plainly refer back to the "plasma ranolazine concentration" to which the rest of the paragraph is directed. The specification uses "ranolazine concentration" and "ranolazine levels" interchangeably. (*Compare* PTX 21 '258 Patent Col. 2:4-5 ("provides therapeutically effective ***plasma concentrations*** of ranolazine") *with* Col. 4:2 ("provide for therapeutic ***plasma levels*** of ranolazine") (emphasis added); Col. 6:60-63 ("it has been found that these methods produce sustained release ranolazine formulations that provide lower peak plasma ***levels*** and yet effective plasma ***concentrations*** of ranolazine . . .") (emphasis added); *see also* 7:62-65; 8:25-27; 10:42-53.) And while Lupin argues that in Examples 6 and 7 the specification's use of "peak plasma levels of 4-6 or 2-4 hours are inconsistent with mean values reported for T_{max}," (Lupin Opening Br. p.3 n1) Lupin is incorrect—there is no inconsistency. Table 6 reflects a range of mean T_{max} values, out to 2 decimal points, from 4.25 to 6.21 and, consistent with the mean values in the

table, the specification states there were "peak plasma levels at 4 to 6 hours post dose." (PTX 21 '258 Patent Col. 16:1-27.) Similarly, Table 7 reflects a range of T_{max} values from 2.00 to 4.33 and, again consistent with the mean values in the table, the specification states there were "peak plasma levels observed at 2 to 4 hours post dose." (PTX 21 '258 Patent Col. 16:42-59.) Thus, contrary to Lupin's assertion, the specification is reporting ***mean values*** in connection with ***plasma levels***.

Second, the fact that plasma levels or plasma concentrations are determined by taking blood from individuals is of no moment. Of course, mean values are obtained from individual blood plasma data. Individual data are a prerequisite to determining a mean value. The specification's description of how ranolazine concentration from individuals is assayed does not change, and is in no way inconsistent with, the specification's explicit statement that ranolazine concentration is a mean value.

The specification governs here—the pharmacokinetic limitations are mean values. The cases Lupin cites to support its "individual patient" construction do not counsel a different result here. *Nautilus Neurosciences, Inc. v. Wockhardt USA LLC*, Nos. 11-1997 (ES), 12-1243 (ES), 2013 WL 775750 (D.N.J. Feb. 27, 2013); *Acorda Therapeutics Inc. v. Apotex Inc.*, No. 07-4937 (GEB-MCA), 2011 WL 4074116 (D.N.J. Sept. 6, 2011); *Wyeth*, 579 F. Supp. 2d 711.

Nautilus involved a means-plus-function claim and the issue was the construction of the function "means for enhancing said average T_{max}". 2013 WL 775750 at *6. Although the Defendants had ***initially*** proposed a construction that included affecting the T_{max} "in more than one patient," at the *Markman* hearing, ***Defendants agreed to adopt Plaintiffs proposed construction*** which involved affecting the T_{max} in "a human patient." *Id.* With no longer a dispute over this term between the parties, the court, not surprisingly, adopted Plaintiffs'

proposed construction. *Id.* at 7. In so doing, the court noted that the Defendants had cited ***no*** intrinsic or extrinsic evidence in support of their initial "more than one patient" proposal. *Id.* The case here is far different. The parties here have not agreed to a construction, and the intrinsic (and extrinsic) evidence is overwhelmingly in support of Plaintiffs' construction.

In *Acorda*, there was no indication from the court that the specification had any description of mean values or any definitions at all related to the disputed claim terms. *See* 2011 WL 4074116 at *1-4. As such, *Acorda* is unhelpful in resolving the parties' dispute.

Finally, as discussed above and in Plaintiffs' opening brief, *Wyeth v. Lupin* demonstrates well why the Court should adopt Plaintiffs' proposed construction.[1] Although the court found, in contrast to the *Wyeth v. Sandoz* court, 703 F. Supp. 2d, 508, 523-24 (E.D. N.C. 2010), that the ordinary meaning of "in a patient" referred to an individual value, the court determined ***based on the specification*** that "[t]he correct understanding of the T_{max} (and C_{max}) values referenced in the claims is that those values refer to an average value taken from multiple individuals." *Wyeth v. Lupin*, 579 F. Supp. 2d at 719. The court explained that the specification contained two tables and presented numbers that were based on the aggregation of the results from multiple individuals. *Id.* Here, not only does every table in the specification present pharmacokinetic values as mean values, the specification contains an express definition that ranolazine plasma concentration is a mean value.

III. CONCLUSION

For the foregoing reasons, Plaintiffs respectfully submit that the peak and trough elements of the asserted claims should be interpreted to refer to mean values.

[1] Lupin's argument that if the reasoning of *Wyeth v. Lupin* is followed here, then this Court can "similarly proceed to invalidate the claims under ¶ 112" has no merit. (Lupin Opening Br. at 4.) In *Wyeth v. Lupin*, the court did not invalidate the claims under ¶ 112, and nothing from that court's decision support's Lupin's new ¶ 112 arguments.

Dated: June 14, 2013

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